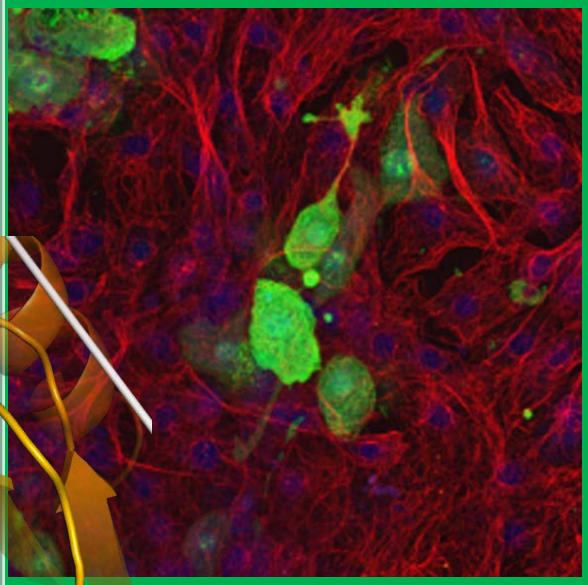
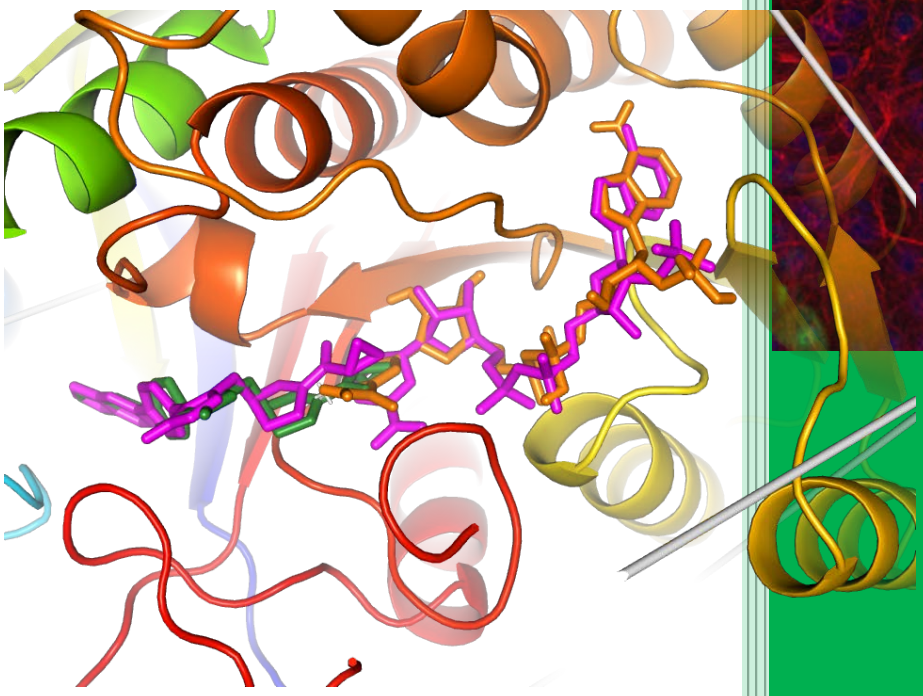
ANNUAL REPORT 2016





INSTITUTE OF MOLECULAR AND CELL BIOLOGY

UNIVERSITY "MIGUEL HERNÁNDEZ"

DIRECTOR'S FOREWORD

The Institute of Molecular and Cell Biology (IBMC) is one of the University Research Institutes at the University *Miguel Hernandez de Elche*. The IBMC is located in the University Campus in Elche, occupying a 4,000 sq. m. of laboratory in the Torregaitán Building. The Institute was created in 2002 from a transformation of the Center of Molecular and Cell Biology, thanks to the initiative and enthusiasm of its inspirator and first Director Prof. José Manuel González-Ros, who had the vision of creating a multidisciplinary research Institute in the University as a wise strategy to carry competitive and transferable research in the fields of Biomedicine and Biotechnology. This devotion to translational research has been a pivotal hallmark of the IBMC since its creation. As a result, in the past 17 years the IBMC has excelled in its scientific production as well as in the exploitation of the results generated by their groups. Furthermore, the interest of transferring the scientific results to society has thrust the creation of spin-off companies and Joint ventures with private enterprises and local Hospitals. This seminal vision has been kept invariable and can be fully appreciated in the Annual Report 2016 that describes all our achievements in research, exploitation, training and dissemination activities. All these accomplisments are in line with the objectives set in our Plan of Action 2013-2017.

Research teams have been very active in securing funding from both governmental and private sources, publishing papers that are widely cited, training young scientists with the highest scientific standards as recognized by the Excellence Mention of our Doctorate program by the Ministry of Education, and to disseminate our activities and achievements to society through our out-reach program. In addition, we have established a Master Degree on Biotechnology and Bioingeneering with the Institute of Bioingeneering that is becoming a reference for the competences and skills tought. Notwithstanding, a major success of the Institute has been the commercialization of innovative products generated from the research projects in the fields of nutraceuticals, cosmeceuticals and biotechnology; and having a lead compound close to enter phase II clinical trials in humans for pain intervention. To reinforce our translational activities, three technological platforms have been stablished. This success has been possible thanks to our philosophy of potentiating collaborations and sharing all the infrastructures, and to the commitment of our administrative and technical personnel to the IBMC project.

Although we have walked a long and fruitful way, there is still plenty to achieve for increasing the IBMC international exposure and scientific distinction. In this regard, our Plan of Action for the next 5 years (2013-2017), strengthens the original vision, and establishes the central mission to consolidate a multidisciplinary program of translational excellence in the areas of biotechnology and health. Since its implementation, we have strictly followed this plan and achieved up to 68% of the planned objectives. We will continue with our comitment to become a reference Institute in the arena of transferable knowledge.

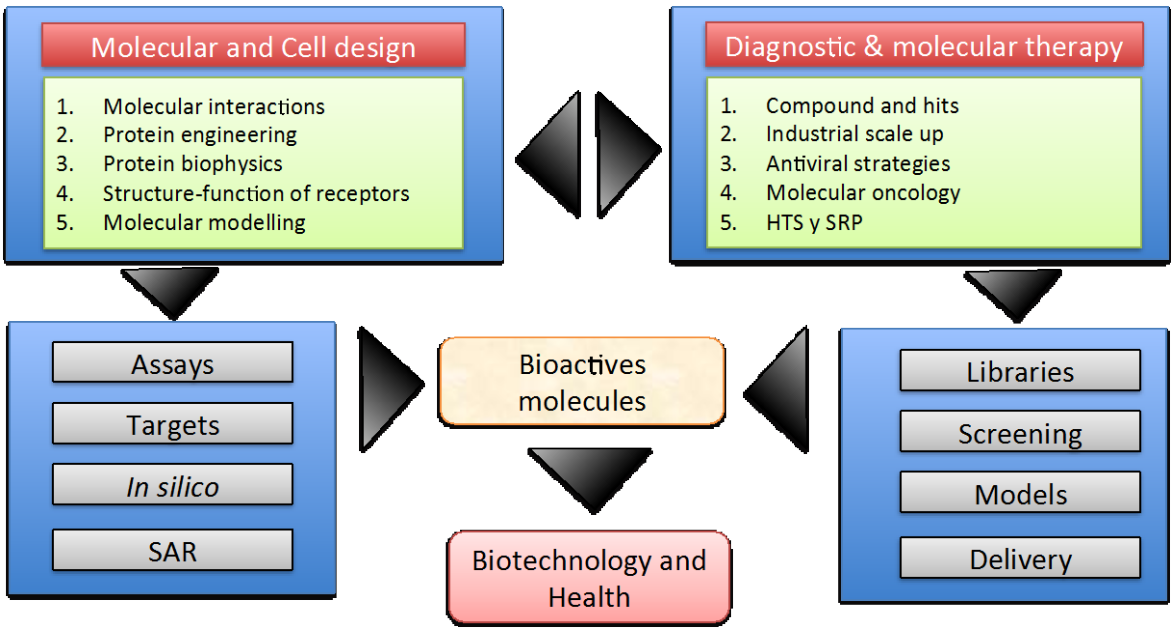
Prof. Antonio Ferrer-Montiel

IBMC Director

STRUCTURE AND GENERAL DESCRIPTION

The IBMC Scientific Program.

The IBMC has established a unique research and training program, which exploits multidisciplinarity, making the most of the complementarities of the groups and using synergies as a strategy for attaining excellence and increasing competitiveness and productivity. To accomplish this aim, in the last two years, research has been organized into two complementary areas of research, namely, (i) ***molecular and cell design*** and (ii) ***molecular diagnosis and therapy***. These research lines, in turn, are organized into sub-areas, which rationally combine the groups' abilities and skills in the supplementary fields that contribute to the development of bioactive molecules, reducing scientific dispersion by grouping activities in order to carry out unique and ambitious research projects. Consequently, in the next five-year period, the IBMC aspires to become a center of reference in the discovery of pharmacological and biotechnological tools, with a clear translational and transfer potential. The intense and sustain work in this line is the central objective for the next five-year period, and to so agreements with PROs will be pursued which will permit reinforcing deficient areas or those that require an impetus for their consolidation, and thereby generating a unique and unprecedented project on a national and international level.



In scientific terms, the targets of these research areas of the IBMC are developed as follows:

A. Molecular and Cellular Design

Research within the line of ***Molecular and Cellular Design*** aims at advancing knowledge of relationships between structure and function in proteins, in order to be able to modify them rationally and specifically. The underlying goal is the transformation of the activity of these proteins with bio and chemo-technological purposes, or the use of the information to design targeted ligands to modulate the receptor activity acting as sensors.

The different scientific backgrounds of the researchers who develop this research line allows a reasonably and pluridisciplinary (though improved) approach to analyze problems, offering an opportunity for the development of common interests and benefiting from synergies that naturally appear in this context. This multidisciplinary approach of issues enables a broad focusing on scientific topics, ranging from a perspective of basic science to investigations with clear translational vocation.

Both the composition of the different research groups that make up this line of research as its multidisciplinarity and flexibility to raise specific scientific goals fosters a high competitiveness, both in the uptake of competitive sources and scientific production, in the training of research personnel and in the technological transfer of research results. In this sense, strong links with research groups both national as international have been notably established, which have materialized, for example,

in leadership or participation in projects coordinated with other institutions both within the different National Plans of Research and funded by the European Union and recently granted.

Molecular and Cellular Design line is organized into two sub-lines, each comprising several research groups with common research interests. The first in centered around ***Molecular Recognition and Protein Biophysics and Engineering***, while the second focuses his research on ***Structure-Function Relationships in Membrane Proteins***.

B. Diagnosis and Molecular Therapy.

The ***Diagnosis and Molecular Therapy*** line seeks the identification and validation of molecular markers in human and animal pathologies of high prevalence, as well as the development of diagnostic methods and therapeutic or preventive strategies. This line consists of a multidisciplinary team of researchers covering from molecular aspects to the semi-industrial production of biological actives.

Milestones achieved in this line of research have had and have a high scientific impact, as shown by scientific publications in magazines of recognized international prestige, as well as the generation of unique technologies that are protected by patents extended worldwide and have been licensed to interested companies. Also, it should be noted as a strong point of this line the high level of national and international collaborations with public bodies and private research, contributing to increase the impact of activities and its internationalization. In addition, the interrelationship of the sub-lines that make up this line of research has fostered identifying synergies and common interests between groups that have driven collaborations that accelerate the achievement of results and technologies.

Clearly, the activities of this line have a high potential for clinical translation materialized in close collaboration with the General Hospital and the University of Elche, as well as biotechnology transfer and exploitation resulting in continuous and consolidated collaborations with biotech, food, cosmetics and pharmaceutical companies.

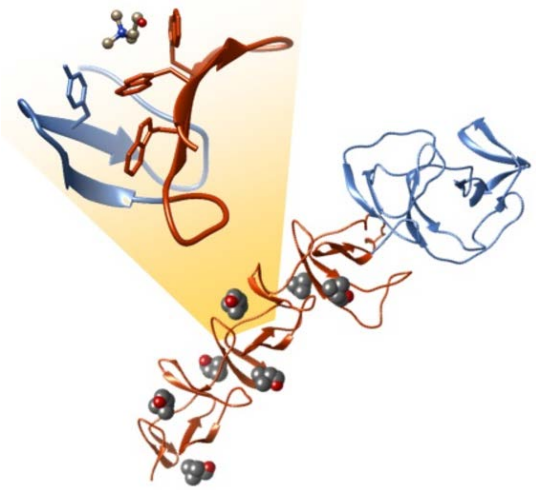
MOLECULAR AND CELLULAR DESIGN LINE.

MOLECULAR AND CELLULAR DESIGN.

Molecular Recognition and Protein Biophysics and Engineering.

Group name: PROTEIN BIOTECHNOLOGY.

We develop basic research on the structure and folding of proteins by the acquisition of structural and thermodynamic data. Many of our results are oriented towards technological transfer, more precisely those dealing with the design of new antibiotics and the setup of novel systems of purification and immobilization of recombinant proteins. Our studies are centered basically in three lines:



1. Design, selection and evaluation of new antimicrobials against Streptococcus pneumoniae (pneumococcus) based on small molecules or in multivalent nanoparticles.

2. The C-LytA affinity tag, that serves as a model to study the folding and engineering of repeat proteins and constitutes an efficient affinity tag for the single-step chromatographic purification and immobilization of recombinant proteins from nano- to macrosurfaces, including enzymatic electrodes.

3.- Bioplastics. Natural, biodegradable plastics of bacterial origin that may constitute an alternative to the use of petroleum derivatives. We study the structure and function of several proteins involved in the synthesis, stability and degradation of these bioplastics, and the immobilization of proteins on these polymers.

Laboratory expertise includes:

- Thermodynamic analysis of protein stability.

- Spectroscopy (absorption, fluorescence, circular dichroism).

- Protein engineering.

- Nanobiotechnology.

Staff.

Jesús Miguel Sanz Morales

Manuel Sánchez Angulo (Visiting scientist)

Postdoctoral scientists.

Beatriz Maestro

Ph.D Students.

Emma Roig Molina

Technicians.

Maite Garzón Cabrerizo

Publications.

Maestro B, Sanz JM. Choline Binding Proteins from Streptococcus pneumoniae: A Dual Role as Enzybiotics and Targets for the Design of New Antimicrobials. Antibiotics (Basel). 2016 Jun 14;5(2). pii: E21

Governmental Projects and Funding.

Programa Estatal De Investigación, Desarrollo E Innovación Orientada A Los Retos De La Sociedad. Ministerio de Economía y Competitividad. "Estructura de proteínas de la superficie de Streptococcus pneumoniae: diseño de nuevas moléculas inactivantes y ensayo como antimicrobianos" (BIO2013-47684-R; 2014-2016). IP: Jesús M. Sanz

Programa Estatal De Investigación, Desarrollo E Innovación Orientada A Los Retos De La Sociedad. Ministerio de Economía y Competitividad. "Remodelacion de la pared celular de Streptococcus pneumoniae: estudios estructurales de las proteinas StkP y LytA como objetivo para el desarrollo de nuevos antimicrobianos (BIO2016-79323-R; 2016-2019). IP: Jesús M. Sanz

Private Funding.

Contract " LIPOENZYM II - Aplicación de la biotecnología en la mejora medioambiental de

los procesos de tintura textil. Funded by AITEX - Instituto Tecnológico Textil (01/07/2016-31/12/2016). IP: Jesús M. Sanz.

Scientific and Educational Commities.

Miembro de tribunal evaluador del programa de Becas de Formación de Personal Investigador del Gobierno Vasco (2015-actualidad). Jesús M. Sanz

Vocal de la Comisión de Acreditación de Ciencias Experimentales de la Agencia de Evaluación del Sistema Universitario Vasco (2015-actualidad) Entidad de realización: Gobierno vasco. Jesús M. Sanz.

Number of Congress Communications.

National contributions: 1

Oral presentations: 1

International contributions: 5

Oral presentations: 4

Poster presentations: 1.

Organization of Meetings.

III Jornadas "Y tú, ¿qué investigas?". Universidad Miguel Hernández. 06/10/2016 - 07/10/2016. Organizador: Jesús M. Sanz.

Editorial Boards.

Member of the Editorial Board of Microbial Biotechnology (Jesús M. Sanz).

Group name: PROTEIN STRUCTURE AND THERMODYNAMICS OF MOLECULAR RECOGNITION.

Our group is involved in the study, by using calorimetric and spectroscopic techniques, of macromolecular interactions. To that end, the group has the expertise in DSC, ITC, fluorescence and circular dichroism. Furthermore, the group has the knowledge to solve structures by using state-of-the-art techniques. Some, but note exclusively, of the biomolecules currently under study in the group are: (i) those involved in the phosphorylation tranfer in micro-organisms; and (ii) those implicated in the aseembly of the capsid of HIV.

Staff.

Javier Gómez-Pérez

José Luis Neira

Postdoctoral Scientists.

Rocío Esquembre Tomé

Ph.D Students.

Felipe Hornos Adán

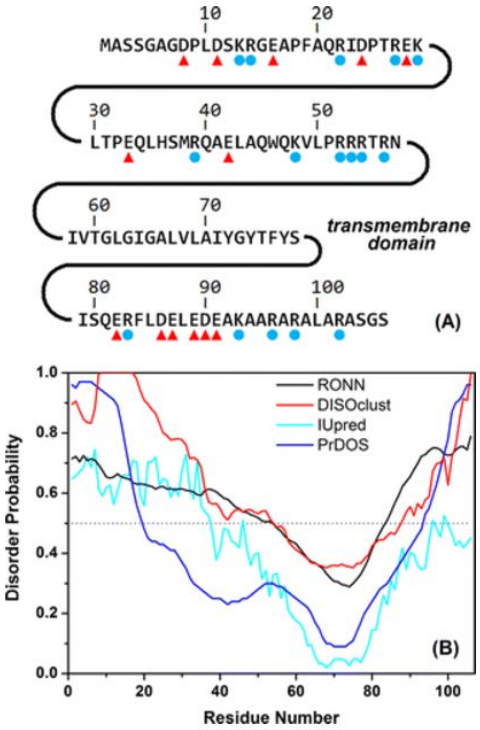
Publications.

Neira JL, Rizzuti B, Iovanna JL. Determinants of the pKa values of ionizable residues in an intrinsically disordered protein. Arch Biochem Biophys. 2016 May 15; 598:18-27.

Neira JL, Hornos F, Bacarizo J, Cámara-Artigás A, Gómez J. The Monomeric Species of the Regulatory Domain of Tyrosine Hydroxylase Has a Low Conformational Stability. Biochemistry. 2016 Jun 21; 55(24):3418-31.

Pantoja-Uceda D, Neira JL, Saelices L, Robles-Rengel R, Florencio FJ, Muro-Pastor MI, Santoro J. Dissecting the Binding between Glutamine Synthetase and Its Two Natively Unfolded Protein Inhibitors. Biochemistry. 2016 Jun 21; 55(24):3370-82.

Neira JL, Medina-Carmona E, Hernández-Cifre JG, Montoliu-Gaya L, Cámara-Artigás A, Seffouh I, Gonnet F, Daniel R, Villegas S, de la Torre JG, Pey AL, Li F. The chondroitin sulfate/dermatan sulfate 4-O-endosulfatase from marine bacterium Vibrio sp FC509 is a dimeric species: Biophysical characterization of an endosulfatase. Biochimie. 2016 Dec; 131:85-95.



Neira JL, Martínez-Rodríguez S, Hernández-Cifre JG, Cámara-Artigas A, Clemente P, Peralta S, Fernández-Moreno MÁ, Garesse R, García de la Torre J, Rizzuti B. Human COA3 Is an Oligomeric Highly Flexible Protein in Solution. Biochemistry. 2016 Nov 15; 55(45):6209-6220.

Governmental Projects and Funding.

CTQ2015 – 64445 - R, Interacciones macromoleculares y "farmacobilidad" de proteinas intrinsicamente desordenadas implicadas en el desarrollo de cancer de pancreas (Macromolecular interacctions and druggability of IDPS involved in pancretaic cancer).

Prometeo 2013/18, Interacciones proteína-polielectrolito: diseño racional de nuevas herramientas en la optimización de procesos biotecnológicos (Polyelectrolites–protein interactions: new tools to optimize biotechnological processes).

Editorial Boards.

Open Enzyme Inhibition Journal (2007-…) José L. Neira (Editorial board).

ISRN Biochemistry (2012-….) José L. Neira (Editorial board).

Archives of Biochemistry and Biophysics (2013-…). José L. Neira (Editor).

Scientific and Educational Commities.

- FWO Flandes (Research Foundation - Flanders (Fonds Wetenschappelijk Onderzoek - Vlaanderen, FWO). José L. Neira.

- CONYCET, Argentina. José L. Neira.

- Israeli Science Foundation. José L. Neira.

- Czech Science Foundation. José L. Neira.

Number of Congress Communications.

National contributions: 1

Oral presentations: 1.

Group name: FLUORESCENT NANOMATERIALS APPLIED TO BIOLOGICAL SYSTEMS.

Our group is interested in the development of new fluorescent materials with applications in biological systems. On one hand, we design and develop fluorescent biosensors with high sensitivity, based on the entrapment of organic molecules and biomolecules in inorganic matrices, and characterize these hybrid materials at a molecular level in order to improve their applications. On the other hand, we work on the design, synthesis and characterization of novel fluorescent conjugated polyfluorenes, to be used as nanoparticles and nanofibers in applications such as bioimaging, drug delivery, clinical diagnosis and sensing devices for biomolecules. Other group activities include the characterization of macromolecular interactions, especially in non-conventional systems, such as ionic liquids as well as the synthesis of conjugated polymers to be applied in photonics and optoelectronics devices.

Staff.

Carmen Reyes Mateo Martínez

Ricardo Mallavia Marin

Mª José Martínez Tomé

Ph.D Students.

Rebeca Vázquez Guilló

Zehra Kahveci

Amalia Mira Picó

Technicians.

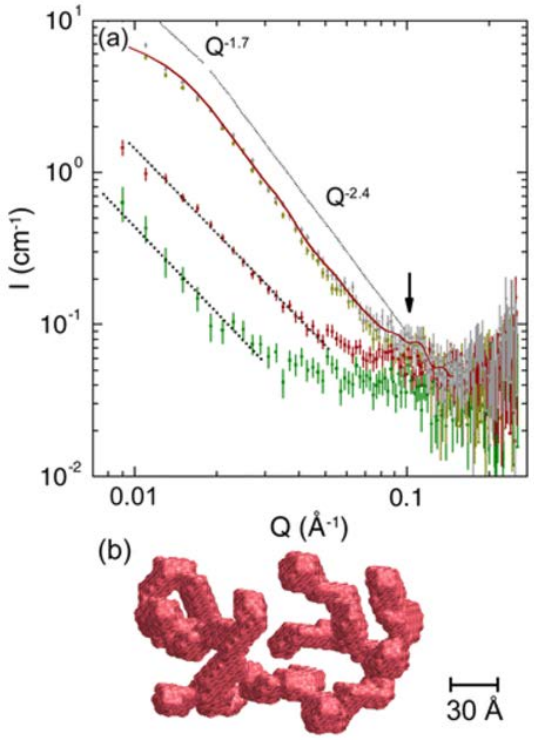
Elisa Pérez García

Publications.

Kahveci Z, Vázquez-Guilló R, Martínez-Tomé MJ, Mallavia R, Mateo CR. New Red-Emitting Conjugated Polyelectrolyte: Stabilization by Interaction with Biomolecules and Potential Use as Drug Carriers and Bioimaging Probes. ACS Appl. Mater. Interfaces, 2016, 8 (3), pp 1958–1969.

Kahveci Z, Vázquez-Guilló R, Mira A, Falcó A, Mallavia R., Mateo CR. Selective recognition and imaging of bacterial model membranes over mammalian ones by using cationic conjugated polyelectrolytes. Analyst 2016,141 (22), 6287-6296.

H.D. Burrows, T. Costa, M.L. Ramos A.J.M. Valente, B. Stewart, L.L.G Justino, A.I.A. Almeida, N.L.Catarina, R. Mallavia and M. Knaapila. Self-assembled systems of water soluble metal 8-hydroxyquinolates with surfactants and conjugated polyelectrolytes for optical sensing, light harvesting and charge transport Physical Chemistry Chemical Physics, 2016, 18 (25), pp 16629-16640.



M. Knaapila, B. Stewart, T. Costa, S.E. Rogers, J. Pragana, S. M. Fonseca, A.J.M. Valente, M.L. Ramos, D. Murtinho, J. Costa Pereira, R. Mallavia and H.D. Burrows. Incorporation of a cationic conjugated polyelectrolyte CPE within an aqueous poly(vinyl alcohol) sol. Macromolecules, 2016, 49 (23), pp 9119-9131..

Science dissemination: outreach activities.

Jornadas de divulgación científica "Ciencia con Tapas".

- ¿Cómo afrontar el Alzheimer? Diagnóstico y cuidados, 11-02-2016.
- ¿Qué sabemos de las adicciones? Aspectos científicos y sociales, 09-06-2016.

- Nuevos alimentos, productos alimenticios y nutracéuticos: novedades que llegaron para quedarse, 13-10-2016.

- Envejecimiento y memoria, 01-12-16.

Mª José Martínez Tomé. Comité organizador.

Jornada de divulgación científica "Ciencia con Tapas" dentro del módulo "Ciencia, salud y tecnología" desarrollado en la II Feria de la Ciencia y la Tecnología en Elche.

- Zika, Ebola y Chikunguña: los virus que salieron del bosque…, 29-04-2016

Mª José Martínez Tomé. Comité organizador.

PhD Theses.

Interaction between Conjugated Polyelectrolytes and Biological Systems: Characterization and Biotechnological Applications. Programa: Doctorado en Biología Molecular y Celular (RD 1393/07). Doctoranda: Zehra Kahveci. Supervisor: C. Reyes Mateo. 4-11-2016.

Governmental Projects and Funding.

Ministerio de Economía y Competitividad. "Desarrollo de nanoestructuras basadas en polielectrolitos para su aplicación como herramientas de diagnóstico, transporte de fármacos y diseño de biosensores" (MAT-2014-53282). IP: R. Mallavia y C. Reyes Mateo.

Proyecto Prometeo. Generalitat Valenciana. "Interacciones proteína-polielectrolito: diseño racional de nuevas herramientas en la optimización de procesos biotecnológicos (PROMETEO 2013/18) (01/01/2013-21/12/2016). IP: J. Gómez.

Number of Congress Communications.

National contributions: 5

Oral presentations: 1

Poster presentations: 4

International contributions: 5

Oral presentations: 1

Poster presentations: 4.

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Structure-Function Relationships in Membrane Proteins.

Group name: STRUCTURE-FUNCTION RELATIONSHIP OF ION CHANNELS.

Structure/Function relationships in membrane proteins: Neuroreceptors and ion channels. Lipid-Protein and Protein-Protein interactions in biological membranes. Modulation of ion channels. Potential applications to drug discovery.

Staff.

José Manuel González-Ros

José Antonio Poveda Larrosa

Postdoctoral Researchers.

Mª Lourdes Renart

Marcela Giudici

Ph.D Students.

Estefania Montoya

Technicians.

Eva Martínez

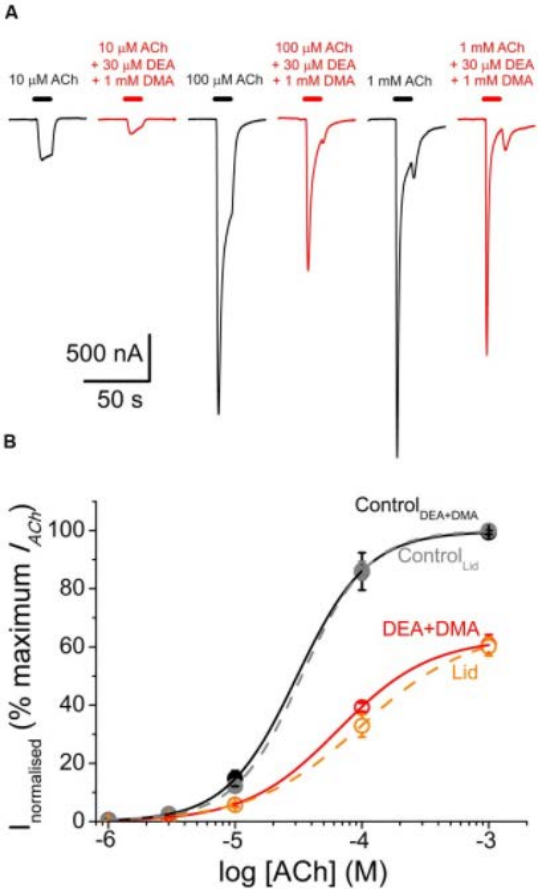
Publications.

Alberola-Die A, Fernández-Ballester G, González-Ros JM, Ivorra I, Morales A. Muscle-Type Nicotinic Receptor Modulation by 2,6-Dimethylaniline, a Molecule Resembling the Hydrophobic Moiety of Lidocaine. Front Mol Neurosci. 2016 Nov 24; 9:127.

Muscle-Type Nicotinic Receptor Blockade by Diethylamine, the Hydrophilic Moiety of Lidocaine. Alberola-Die A, Fernández-Ballester G, González-Ros JM, Ivorra I, Morales A. Front Mol Neurosci. 2016 Feb 15; 9:12.

PhD Theses.

Relación estructura-función en el canal de potasio procariota KcsA. Doctoranda: Estefanía Montoya Díaz. Supervisor: José Manuel González-Ros, Asia Fernández-Carvajal y Jose Antonio Poveda.



Governmental Projects and Funding.

Funding entity: Spanish "Ministerio de Economía y competitividad". Reference: BFU2015-66612-P. Title: Molecular basis of ion channel modulation. Dates: 01/01/2016 - 31/12/2018. Grant: 124.509,00 €. Group leader: José Manuel González-Ros and José Antonio Poveda Larrosa. Number of researchers: 4.

Number of Congress Communications.

International contributions: 1

Poster presentations: 1

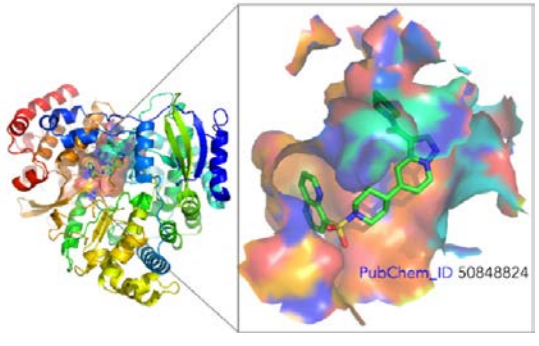
Molecular modeling platform.

Group name: STRUCTURAL BIOCOMPUTING.

The platform for molecular modeling and virtual screening arises as a unit that brings the capabilities of groups in bioinformatics methods based on biomolecular structures. Its mission is to integrate efforts to the use (databases) or the construction of macromolecular structures (homology modeling) to be used for rational protein modification (computer design), to determine protein interaction maps (protein-protein interactions), or to identify novel active compounds (molecular docking and virtual screening) from libraries of compounds (chemical libraries). Additionally, simulation (Molecular Dynamics) recreates the macromolecules in their native environment, including lipids, water and ions.

The high resolution (3D) structural data are used to extract useful information about protein-protein interactions to elucidate protein interaction networks, and to understand the formation of the macromolecular complex. The modeling of macromolecular structures, in which the target is treated as a single molecule or a ligand-receptor complex, allows the determination of structure-function relationships of the soluble and membrane proteins, mechanical molecular simulations of complex systems, the binding ligand, or even enzyme mechanism.

For this purpose, there is dedicated room endowed with an air-conditioned machine and a proper electrical installation to house two high performance servers and two "cluster" of computers with 182 processors, as well as the programs needed to address the management, editing and modification of macromolecules.



The combination of the experimental techniques of high throughput screening (HTS) with computational techniques and virtual screening bioinformatics open ways for high performance research, because the computational in silico calculations determine quickly and economically those families of compounds capable of exerting a biological effect with the chosen targets, whereas with experimental screening techniques the parameters of interaction between ligands and receptors are quantified. Once certain lead compounds, and again using computational techniques, the ligands can be redesigned to increase the specificity of action, the affinity, or both.

Staff.

Gregorio Fernández-Ballester (IBMC-UMH).

José Antonio Encinar (IBMC-UMH).

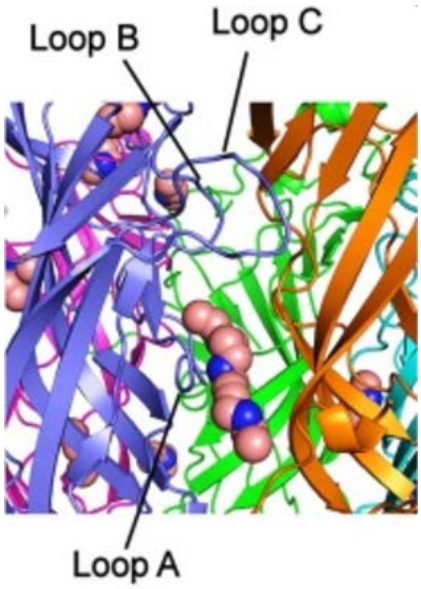
Vicente Galiano Ibarra (Departamento de Física y Arquitectura de Computadores, UMH).

Ph.D Students.

Magdalena Nikolaeva Koleva

Publications.

Galiano-Ibarra, V., Garcia-Valtanen, P., Micol, V., Encinar, J.A. Looking for inhibitors of the Dengue virus NS5 RNA-dependent RNA-polymerase using a molecular docking approach. Drug Design, Development and Therapy 2016, 10: 3163-3181.



Bello, M., Falco, A., Medina Gali, R.M., Encinar, J.A., Novoa, B., Perez, L., Coll, J. Structure and functionalities of the human c-reactive protein compared to the zebrafish multigene family of c-reactive-like proteins. Dev Comp Immunol. 2016; 69:33-40.

Alberola-Die A, Fernández-Ballester G, González-Ros JM, Ivorra I, Morales A. Muscle-Type Nicotinic Receptor Modulation by 2,6-Dimethylaniline, a Molecule Resembling the Hydrophobic Moiety of Lidocaine. Front Mol Neurosci. 2016 Nov 24; 9:127.

Muscle-Type Nicotinic Receptor Blockade by Diethylamine, the Hydrophilic Moiety of Lidocaine. Alberola-Die A, Fernández-Ballester G, González-Ros JM, Ivorra I, Morales A. Front Mol Neurosci. 2016 Feb 15; 9:12.

Governmental Projects and Funding.

Título: Searching for applications of fish innate memory ("trained immunity"): immunomodulators, therapeutic agents and vaccines. Convocatoria 2014 - Proyectos I+D+I - Programa Estatal de Investigación, Desarrollo e Innovación orientada a los retos de la sociedad. Ref.: AGL2014-51773-C3-1-R. N° invest. 3. Investigador coordinador: Dr. Luiz Pérez. Subvención concedida: 140.000 euros. Fechas: 2015-2017. Entidad financiadora: Ministerio de Ciencia e Innovación. Investigador: J.A. Encinar.

Título: Nutraceúticos de 2ª generación de plantas comestibles basados en extractos polifenólicos moduladores del metabolismo energético: aplicaciones en la prevención de la obesidad. Convocatoria 2016 - Proyectos I+D+I - Programa Estatal de Investigación, Desarrollo e Innovación orientada a los retos de la sociedad. Ref.: AGL2015-67995-C3-1-R. N° invest. 3. Investigador coordinador: Dr. Vicente Micol. Subvención concedida: 127.050 euros. Fechas: 2016-2018. Entidad financiadora: Ministerio de Ciencia e Innovación. Investigador: J.A. Encinar.

Título: El carácter multifactorial de los polifenoles: una oportunidad para el desarrollo de herramientas terapéuticas frente a la obesidad y las enfermedades infecciosas. Ref.: PROMETEO/2016/006. N° invest. 6. Investigador coordinador: Dr. Vicente Micol. Subvención concedida: 219.478 euros. Fechas: 2016-2019. Entidad financiadora: Ministerio de Ciencia e Innovación. Investigador: J.A. Encinar.

Sensibilización algésica de nociceptores en dolor crónico: mecanismos e intervención farmacológia. 23/06/2015 - Proyectos de I+D+I "Retos de la Sociedad" - MINECO 2015 (SAF2015-66275-C2-1-R). Coordinator: Antonio Ferrer Montiel. UMH-CSIC Ministerio de Economia y Competitividad. Investigador: G. Fernández-Ballester.

Private funding: Contracts.

Contrato para la realización del trabajo "Modelización molecular de interacciones proteína-proteína en el receptor muscarínico de acetilcolina". Funded by Antalgenics SL (ANTALGENICS2.15T; 30/04/2016). IP: G. Fernandez-Ballester.

Adenda al contrato para la realización del trabajo "Modelización molecular de interacciones proteína-proteína en el receptor muscarínico de acetilcolina". Funded by Antalgenics SL (ANTALGENICS4.16D; 28/10/2016). IP: G. Fernandez-Ballester.

Scientific and Educational Commities.

Agencia Nacional de Evaluación de la Calidad y Acreditación (ANECA). J.A. Encinar.

Number of Congress Communications.

International contributions: 3

Poster presentations: 5

MOLECULAR DIAGNOSIS AND THERAPY LINE.

MOLECULAR DIAGNOSIS AND THERAPY.

Bioactive Molecules.

Group name: NATURAL BIOACTIVE COMPOUNDS.

The relationship between the biological activity of natural dietary compounds and its effects on chronic human diseases is under intense debate. The research target of our group is to characterize the wide biological activity of natural bioactive compounds using cellular and animal models and to understand the mechanism underlying their health effects. The characterization and identification of natural compounds in complex matrixes, especially polyphenols, is also our target. Our group is focused on:

The capacity of polyphenols to ameliorate metabolic disturbances associated to obesity (oxidative stress and insulin resistance) in cellular models and hyperlipidemic mice.

Bioguided screening of antimicrobial herbal extracts and compounds for applications in cosmetics, hygiene or medical devices. Searching for natural compounds for dermocosmetic applications.

The antiproliferative and apoptotic effects of polyphenols in cancer cellular models using global OMICs. Nano-encapsulation of potential anticarcinogenic compounds.

Characterization of food and herbal materials by chromatography coupled to mass spectrometry. Semi-industrial scale production of herbal extracts deriving from plants or vegetal by-products.

Optimization of juice extraction processes and integral exploitation of by-products.

Personal.

Vicente Micol Molina, IP

Domingo Saura López

Nuria Martí Bruña

Enrique Barrajón Catalán

Manuel Valero Roche

María Herranz López

Postdoctoral Fellows.

Salud Vegara Gómez

Ph.D Students.

Almudena Pérez López

Verónica Ruiz Torres

Mariló Olivares Vicente

Luz Agulló Chazarra

Sara Gea Botella

Technicians.

Mª Teresa Garzón Cabrerizo

Publications.

Del Mar Contreras M, Borrás-Linares I, Herranz-López M, Micol V, Segura-Carretero A. Further exploring the absorption and enterocyte metabolism of quercetin forms in tha Caco-2 model using nano-LC-TOF-MS. Electrophoresis 37(7-8):998-1006 (2016).

Barrajón-Catalán, E., Morales-Soto, A., Tomás-Menor, L., Segura-Carretero, A., Micol, V. Rockroses (*Cistus sp.*) oils (Chapter 74). In: Preedy, V.R. (Ed.), Essential Oils in Food Preservation, Flavor and Safety. Academic Press, Elsevier Inc. 649–658. ISBN: 978-0-12-416641-7 (2016)

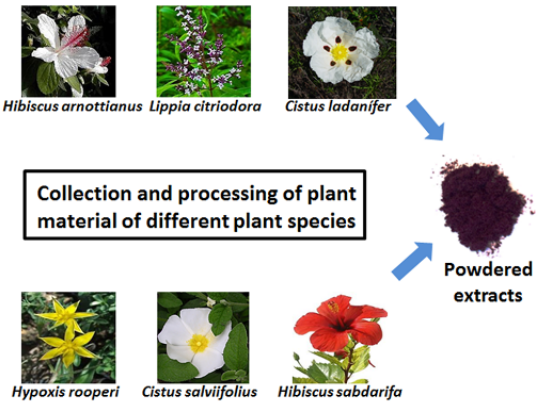
Nobile V, Michelotti A, Cestone E, Caturla N, Castillo J, Benavente-García O, Pérez-Sánchez A, Micol V. Skin photoprotective and antiageing effects of a combination of rosemary (*Rosmarinus officinalis*) and grapefruit (*Citrus paradisi*) polyphenols. Food Nutr Res. 60:31871 (2016).

Pérez-Sánchez A, Barrajón-Catalán E, Herranz-López M, Castillo J, Micol V. Lemon balm extract (*Melissa officinalis, L.*) promotes melanogenesis and prevents UVB-induced oxidative stress and DNA damage in a skin cell model. J Dermatol Sci. 84:169-177 (2016).

Cuyàs E, Pérez-Sánchez A, Micol V, Menendez JA, Bosch-Barrera J. STAT3-targeted treatment with silibinin overcomes the acquired resistance to crizotinib in ALK-rearranged lung cancer. Cell Cycle 15(24):3413-3418 (2016).

Galiano, V., García-Valtanen, P., Micol, V., Encinar, J.A. Looking for inhibitors of the dengue virus NS5 RNA-dependent RNA-polymerase using a molecular docking approach. Drug Design, Development and Therapy 10:3163-3181 (2016).

Cádiz-Gurrea, ML, Alañón-Pardo, E., Arráez-Román, D., Fernández-Arroyo, S., Micol, V. Roche, E., Segura-Carretero, A. Bioactive compounds from *Lippia citriodora*: Application in diseases prevention. In: Occurrences, Structure, Biosynthesis, and Health Benefits Based on Their Evidences of Medicinal Phytochemicals in Vegetables and Fruits (Vol. 7). Motohashi, N. (series editor). Nova Science Publishers, NY, USA. 2016.



Tyc, O., Tomás-Menor, L., Garbeva, P., Barrajón-Catalán, E., Micol, V. Validation of the AlamarBlue® Assay as a Fast Screening Method to Determine the Antimicrobial Activity of Botanical Extracts. PLoS One 11(12):e0169090 (2016).

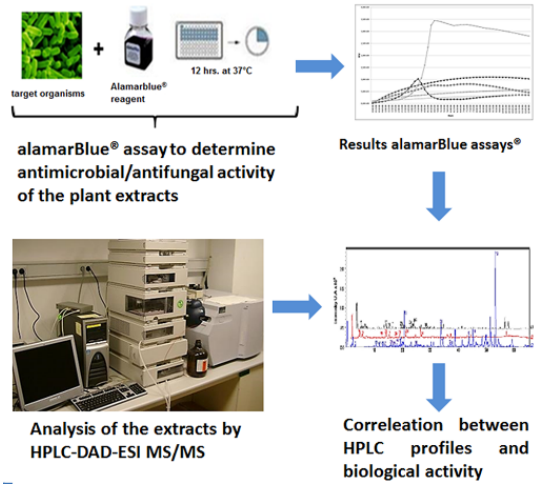
Barrajón-Catalán, E., Funes, L., Herranz-López, M., González-Álvarez, I., Bermejo, M., Micol, V. Curcumin. Clinical Uses, Health Effects and Potential Complications. In: Curcumin. Clinical uses, health effects and potential applications, p 99-110. Martin, V (Editor). NOVA PUBLISHERS. ISBN: 978-1-63484-272-3 (2016).

Cruz, L., Clemente, G., Mulet, A., Ahmad-Qasem, MH, Barrajón-Catalán, E., García-Pérez, JV. Air-borne ultrasonic application in the drying of grape skin: Kinetic and quality considerations. Journal of Food Engineering 168:251-8 (2016).

Khemakhem, I., Ahmad-Qasem, MH, Barrajón-Catalán, E., Micol, V., García-Pérez, JV., Ayadi, MA, Bouaziz, M. Kinetic improvement of olive leaves' bioactive compounds extraction by using power ultrasound in a wide temperature range. Ultrasonic Sonochemistry, 34: 466-73 (2016).

Berenguer, M., Vegara, S., Barrajón, E., Saura, D., Valero, M., Martí N. Physicochemical characterization of pomegranate wines fermented with three different Saccharomyces cerevisiae yeast strains. Food Chem. 190:848-55 (2016).

Pérez-Vázquez, M.T., Hurtado-Pomares, M., Hernández Sánchez, S., Marti, N. Capítulo 44. Universidad Saludable Y Gastronomía Unidas en una Propuesta de la Universidad Miguel Hernández. En Teófilo Sanfeliu Montolio. Más allá de la geología. Libro Homenaje. Volumen 4 de Col·lecció Homenatges. 2016. Publicacions de la Universitat Jaume I, Servei de Comunicació i Publicacions. Universitat Jaume I. 365-368. I.S.B.N 978-84-16356-15-7.



Patents.

Inventores: Saura, D., Marti, N., Valero, M., Vegara-Gomez, S., Berenguer-Martinez, M.D.R., Micol, V, Funes Gómez, L.L., Barrajón-Catalán, E., Martínez-Font, R., Mena Parreño, P. Titulo: Método de producción de pectina modificada de cítricos. Titular: Mitra Sol Tech. Registros: ES2537926. Fecha concesión: 21/04/2016.

Inventores: Domingo Saura, Nuria Martí, Manuel Valero, Salud Vegara, Mª Remedios Berenguer, Vicente Micol. Titulo: Equipo de expansión instantánea a vacío y ultrasonidos. Titular: UMH, Mitra Sol Tech. Registros: PCT/ES2013/000191 (Fecha solicitud: 09/08/2012). Fecha concesión: 05/02/2016. Referencia Patente: P201200830; W02014-170347 (A1).

Inventores: Saura, D. Marti, N. Valero, M. Vegara-Gomez, S. Berenguer-Martinez, M.D.R., Micol, V, Bernal Belda, E. Titulo: Apparatus for instantaneous expansion with vacuum and ultrasound waves. Titular: Mitra Sol Tech. Registros: EP 2915437 (A1), EP 2915437 (A4).

Inventores: Saura, D. Marti, N. Valero, M. Vegara Gomez, S. Berenguer Martinez,

M.D.R., Micol, V, Bernal Belda, E. Titulo: Apparatus for instantaneous expansion with vacuum and ultrasound waves. Titular: Mitra Sol Tech. Registros: WO2014023863 (A1), WO2014023863 (A9).

Inventores: Saura, D. Marti, N. Valero, M. Vegara Gomez, S. Barrajón-Catalán, E., Berenguer-Martinez, M.D.R., Micol, V, Bernal-Belda, E. Titulo: Apparatus for instantaneous expansion with vacuum and ultrasound waves. Titular: Mitra Sol Tech. Registros: US 9345795 B2, US 20150258225 (A1)(A4).

Science Communication: Invited talks and courses.

Novel solutions in skin beauty. V. Micol. Vitafoods Europe 2016. The Global Nutraceutical Event. Ginebra (Suiza), 10/05/2016.

Nanoencapsulation of pomegranate bioactive compounds for nutricosmetics. N. Marti, N. O65. International Society of Nutraceuticals & Functional Foods, ISNFF Conference and Exhibition. Rosen Shingle Creek Hotel. Orlando, FL, USA. October 9-13, 2016.

Science dissemination: outreach activities.

"Nuevos alimentos, productos alimenticios y nutracéuticos: novedades que llegaron para quedarse". José Ángel Pérez, Belén Ropero, Vicente Micol. Ciencia con tapas. FNAC, Alicante. (13/10/2016).

"El estrés oxidativo como arma antitumoral". Enrique Barrajón-Catalán. II JORNADAS INVESTIGACION BIOMEDICA. Hospital General Universitario de Elche (03/10/2016).

"Efecto de polifenoles de la dieta sobre parámetros de estrés oxidativo en obesidad". María Herranz-López. II JORNADAS INVESTIGACION BIOMEDICA. Hospital General Universitario de Elche (03/10/2016).

"Desarrollo de Nutracéuticos para el control de peso: de la bancada al mercado". María Herranz-López. Jornada científica del IBMC (14/07/2016).

Governmental Projects and Funding.

Título del proyecto: Nutraceúticos de 2ª generación de plantas comestibles basados en extractos polifenólicos moduladores del metabolismo energético: aplicaciones en la prevención de la obesidad. Entidad financiadora: Dirección General de Investigación. MICINN (AGL2015 – 67995 - C3-1-R). Proyecto coordinado. 127.050 €. 01/01/2016 - 31/12/2018. Investigador responsable y coordinador: Vicente Micol.

Título del proyecto: El carácter multifactorial de los polifenoles: una oportunidad para el desarrollo de herramientas terapéuticas frente a la obesidad y las enfermedades infecciosas. Entidad financiadora: Conselleria de Educación, Formación y Empleo (GV). PROMETEO/2012/007. 51.050 € (2016), 62.655 € (2017), 43.738 € (2018), 62.034 € (2019). Total: 219.477 €. 01/01/2016 – 31/12/2019. Investigador responsable: Vicente Micol.

Título del proyecto: Vesiculas de origen vegetal (bróculi) para la protección y vehiculización de compuestos bioactivos en bebidas y formulaciones dermatologicas de granada. Entidad financiadora: Dirección General de Investigación. Ministerio de Economia y Competitividad (MICINN) AGL2012 – 40175 - C02 - 02. Investigador Responsable: Nuria Martí. 01/01/2013-31/12/2016.

Private funding: Contracts.

Título del proyecto: Contrato para la realización del proyecto CDTI: "Investigación y desarrollo experimental de nuevos alimentos más saludables y envases avanzados". Entidad financiadora: MONTELOEDER, SL. 120.000 €. 01/09/2015-01/09/2019. Investigador responsable: Vicente Micol.

Título del proyecto: Contrato para la realización del proyecto "Investigación Industrial y Desarrollo Experimental de Alimentos Inteligentes". CIEN 2014. CDTI. Entidad financiadora: NUTRAFUR, SA. 15.000 €. 01/02/2015 - 30/06/2016. Investigador responsable: Vicente Micol.

Título del proyecto: Contrato para la ejecución del proyecto "Desarrollo de diferentes aplicaciones de las resinas en el aislamiento de sustancias activas". Entidad financiadora: MITRA SOL TECHNOLOGIES SL. 8.763 €. 22/12/2015 - 21/12/2016. Investigador responsable: Domingo Saura.

Título del proyecto: Contrato para la realización del proyecto "Caracterización y ajustes de formulación de zumos de frutas, verduras, formulación y mezcla de los

mismos, así como del aprovechamiento de residuos". Entidad financiadora: MITRA SOL TECHNOLOGIES SL. 7.500 €. 18/09/2015 - 17/09/2016. Investigador responsable: Domingo Saura.

Título del proyecto: Contrato para la realización del proyecto "Desarrollo de estrategias antimicrobianas y de esterilización". Entidad financiadora: MITRA SOL TECHNOLOGIES SL. 11.250 €. 28/11/2016 - 27/11/2017. Investigador responsable: Domingo Saura.

Título del proyecto: Contrato para la realización del trabajo "Caracterización de preparaciones a base de extractos de uso agrícola como biofertilizantes y biocidas". Entidad financiadora: AGROZYMES SL. 4.050 €. 22/11/2016 - 21/05/2017. Investigador responsable: Domingo Saura.

Título del proyecto: Contrato para la ejecución del proyecto "Desarrollo de diferentes aplicaciones de las resinas en el aislamiento de sustancias activas". Entidad financiadora: MITRA SOL TECHNOLOGIES SL. 8.763 €. 22/12/2015 - 21/12/2016. Investigador responsable: Domingo Saura.

Título del proyecto: Adenda al contrato para la realización del trabajo "Caracterización de la composición de nuevos ingredientes funcionales y determinación de bioactividad para los sectores nutracéutico y cosmético". Entidad financiadora: INVITROTECNIA SL. 4.700 €. 11/06/2015 - 10/06/2016. Investigador responsable: Vicente Micol.

Technical Services and Assistance.

Título del proyecto: Análisis cromatográfico y de propiedades fisicoquímicas. Entidad financiadora: BIOPATNER SL. 1782,20 €. 02/02/2016 - 02/05/2016. Investigador responsable: Enrique Barrajón Catalán.

Título del proyecto: Extracción de principios activos a pattir de matrices alimentarias (gominolas) y cuantificación del contenido en polifenoles totales mediante método de FOLIN. Entidad financiadora: DAMEL. 400 € 22/07/2016 - 22/08/2016. Investigador responsable: Enrique Barrajón Catalán.

Título del proyecto: Evaluación del proyecto de I+D+i 468.431 - Investigación y desarrollo de sistemas de factores de comunicación potenciadores de la regeneración celular. Entidad financiadora: EQA S.L. 750 €. 25/10/2016 - 31/03/2017. Investigador responsable: Enrique Barrajón Catalán.

Título del proyecto: Ajuste de pH, concentrado mediante rotavapor y posterior secado en estufa a vacío. Entidad financiadora: Sharda. 43,50 €. 13/04/2016 - 31/04/2016. Investigador responsable: Enrique Barrajón Catalán.

Título del proyecto: Ensayo de determinación de la presencia de alcaloides según la Farmacopea y compra del patrón de oxinitrato de bismuto. Entidad financiadora: Anastore. 119,90 €. 10/06/2016 - 10/07/2016. Investigador responsable: Enrique Barrajón Catalán.

Título del proyecto: Ensayo de cuantificación de flavonoides y ensayo de cuantificación de taninos. Entidad financiadora: Farmacia Eulogio Taverner. 159 €. 15/06/2016 - 15/07/2016. Investigador responsable: Enrique Barrajón Catalán.

R&D and Educational Committees.

Enrique Barrajón Catalán. Vocal científico en Órgano Evaluador de Proyectos (órgano habilitado) de la Universidad Miguel Hernández de Elche.

Vicente Micol. Evaluador de la Agencia Nacional de Evaluación y Prospectiva (ANEP) (2014-2016).

R&D Management.

Scientific Advisor MONTELOEDER, SL (2002-2016). V. Micol.

Scientific Advisor Mitra Sol Technologies (2015-2016). V. Micol.

Scientific Advisor Mitra Sol Technologies (2015-2016). D. Saura.

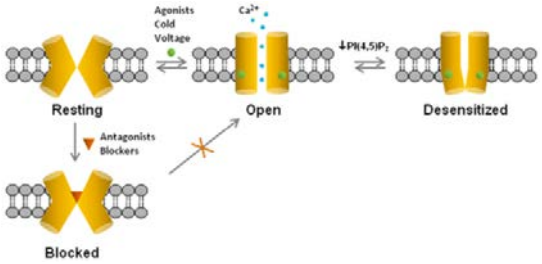
Scientific Advisor Mitra Sol Technologies (2015-2016). N. Martí.

Editorial Boards.

AgroFood Industry Hi-Tech. TeknoScienze. V. Micol.

Group name: DRUG DESING ON THERMOTRPs AND PAIN SIGNALLING.

Our group is interested in understanding the cellular and molecular basis underlying pain transduction in the peripheral nervous system, and to use this knowledge to design and validate novel therapeutic strategies for pain control. Our research is hypothesis-based and combines cellular and molecular approaches, using from animal models to purified proteins. Identification of the signalplexes involved in sensory and pain transduction allows us to identify new druggable targets that enter our drug discovery program for hit identification.



To refine lead development, we are also interested in unveiling the protein structure of the selected targets, mostly thermoreceptor channels (thermoTRPs). This information is essential for accelerating the identification and development of lead compounds. Complementarily, we also characterize the biophysics of channel activity to further understand how ion channels work in terms of their underlying protein structure and the antagonists modulate their activity.

Staff.

Antonio Ferrer-Montiel.

Gregorio Fernández-Ballester

Asia Fernández Carvajal

Postdoctoral Fellows.

Clotilde Ferrándiz

Jan-Albert Manenschijn

Ph.D Students.

Christoph Wolf Jakob

Maite Artero Morales

Verónica Rivero Hernández

Technicians.

Gema Osuna Tenorio

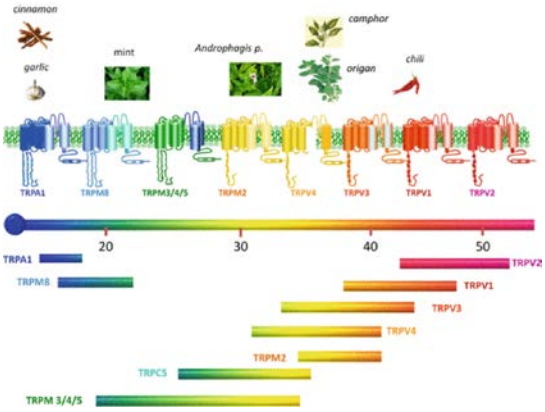
Antonio Manuel Zafra Pinto

Publications.

Mathivanan S, de la Torre-Martinez R, Wolf C, Mangano G, Polenzani L, Milanese C, Ferrer-Montiel A. Efect of econazole and benzydamine on sensory neurons in culture. J Physiol Pharmacol. 2016 Dec; 67(6):851-858.

Vázquez-Jiménez L, Garrido M, Miceli M, Prats E, Ferrer-Montiel A, Teixidó M, Jimeno C, Messeguer A. Synthesis and in vitro, ex-vivo and in vivo activity of hybrid compounds linking a potent ROS and RNS scavenger activity with diverse substrates addressed to pass across the blood-brain barrier. Eur J Med Chem. 2016 Nov 10; 123:788-802. doi: 10.1016/j.ejmech.2016.08.007.

Lakomá J, Rimondini R, Ferrer Montiel A, Donadio V, Liguori R, Caprini M. Increased expression of Trpv1 in peripheral terminals mediates thermal nociception in Fabry disease mouse model. Mol Pain. 2016 Aug 16; 12. pii: 1744806916663729. doi: 10.1177/1744806916663729.



Mathivanan S, Devesa I, Changeux JP, Ferrer-Montiel A. Bradykinin Induces TRPV1 Exocytotic Recruitment in Peptidergic Nociceptors. Front Pharmacol. 2016 Jun 23; 7:178. doi: 10.3389/fphar.2016.00178.

Pérez de Vega MJ, Gómez-Monterrey I, Ferrer-Montiel A, González-Muñiz R. Transient Receptor Potential Melastatin 8 Channel (TRPM8) Modulation: Cool Entryway for Treating Pain and Cancer. J Med Chem. 2016 Nov 23;59(22):10006-10029.

A Bertamino, C Ostacolo, P Ambrosino, S Musella, V Di Sarno, T Ciaglia, M V Soldovieri, N Iraci, A Fernandez Carvajal, R de la Torre-Martinez, A Ferrer-Montiel, R Gonzalez Muñiz, E Novellino, M Taglialatela, P Campiglia, I Gomez-Monterrey. (2016) Tryptamine-based derivatives as Transient Receptor Potential

Melastatin type-8 (TRPM8) channel modulators. Journal of Medicinal Chemistry 2016 Mar 10;59(5):2179-91 PMID:26847872 (12-12-2015/15-01-2016).

P Pérez Faginas, M. T Aranda, R de la Torre-Martinez, S Quirce, A Fernández-Carvajal, A Ferrer-Montiel, 7 (2016). New transient receptor potential TRPV1, TRPM8 and TRPA1 channel antagonists from a single linear β,γ-diamino ester scaffold. RSC Advances, 6, 6868–6877.

M Criado, B Balsera, J Mulet, S Sala, F Sala, R de la Torre Martinez, A Fernández-Carvajal, A Ferrer-Montiel, Moreno-Fernández, S, Miguel, M; M G. López, M J Pérez de Vega and R González-Muñiz (2016). 1,3-Diphenylpropan-1-one Derivatives as Allosteric Modulators of α7 nACh Receptors with Analgesic and Antioxidant Properties. Future Medicinal Chemistry 8(7):731-49. doi: 10.4155/fmc-2015-0001. (26-11-2015/09-03-2016).

Taberner FJ, Devesa I, Ferrer-Montiel A. Calcium Entry Through Thermosensory Channels. Adv Exp Med Biol. 2016; 898:265-304. doi: 10.1007/978-3-319-26974-0_12. Review.

Guiretti D, Sempere A, Lopez-Atalaya JP, Ferrer-Montiel A, Barco A, Valor LM. Specific promoter deacetylation of histone H3 is conserved across mouse models of Huntington's disease in the absence of bulk changes. Neurobiol Dis. 2016 May; 89:190-201. doi: 10.1016/j.nbd.2016.02.004.

Ciardo MG, Andrés-Bordería A, Cuesta N, Valente P, Camprubí-Robles M, Yang J, Planells-Cases R, Ferrer-Montiel A. Whirlin increases TRPV1 channel expression and cellular stability. Biochim Biophys Acta. 2016 Jan;1863(1):115-27. doi: 10.1016/j.bbamcr.2015.10.016.

de la Peña E, Gomis A, Ferrer-Montiel A, Belmonte C. TRPV1 channel modulation by hyaluronan reduces pain. Channels (Austin). 2016;10(2):81-2. doi: 10.1080/19336950.2015.1109300.

A. Alberola-Die; G. Fernandez-Ballester; J.M. González-Ros; I. Ivorra; and A. Morales. (2016). Muscle-type nicotinic receptor blockade by diethylamine, the hydrophilic moiety of lidocaine. Frontiers in Molecular Neuroscience. 9:12. pp:1-12. doi: 10.3389/fnmol.2016.00012.

A. Alberola-Die; G. Fernandez-Ballester; J.M. González-Ros; I. Ivorra; and A. Morales. (2016). Muscle-Type Nicotinic Receptor Modulation by 2,6-Dimethylaniline, a Molecule Resembling the Hydrophobic Moiety of Lidocaine. Frontiers in Molecular Neuroscience. 9:127 pp: 1-16. doi 10.3389/fnmol.2016.00127.

Creation of Spin-Off Firms.

Antonio Ferrer. Named administrator of PROSPERA BIOTECH and FASTBASE SOLUTIONS.

Patents.

Inventores: Gonzalez Muñoz R. (CSIC), Bonache De Marcos M.A. (CSIC), Antonio Ferrer Montiel (Universidad Miguel Hernández), Asia Fernández Carvajal (Universidad Miguel Hernández), Roberto de la Torre (Universidad Miguel Hernández). Título: Heterocyclic compounds as trpm8 channel antagonists and uses thereof. Titular: UMH (50%), CSIC (50%). Registros: PCT/ES2016/070483 (29/06/2016) WO2017005950 A1.

PhD Theses.

Characterization and evaluation of TRPV1 and TRPM8 antagonists as potential therapeutic tools for treating pain. Roberto de la Torre Martínez. Supervisor: Asia Fernández-Carvajal y Antonio Ferrer-Montiel. 11 julio 2016.

Estudios de conducción y selectividad iónicas basados en un canal de potasio modelo: KcsA. Estefanía Montoya Díaz Supervisor: Asia Fernández-Carvajal, Jose Antonio Poveda y Jose Manuel Gonzalez Ros. 29 julio 2016.

Identification and characterization of Whirlin as a novel modulator of TRPV1. Maria Grazia Ciardo. Supervisors. Antonio Ferrer Montiel and Rosa Planells Cases. 22 enero 2016.

Differential mechanisms of TRPV1 sensitization in peptidergic and nonpeptidergid nociceptors. Shaktikumar Mathivanan. Supervisor. Antonio Ferrer Montiel. 12 mayo 2016.

Organization of Meetings.

5th. International Iberian Congress on Biophysics.15-17th June. Porto. Portugal.

Invited Talks and Courses.

39th Congreso de la SEBBM. Conferencia: Aprendiendo del fracaso en emprendimiento. Foro del Emprendedor. Salamanca (Spain). Septiembre, 2016.

Science Dissemination: Outreach Activities.

Ciencia con Tapas. Monthly outreach activity of IBMC.

Governmental Projects and Funding.

Fisiopatología neurosensorial: mecanismos e intervención terapéutica. Generalitat Valenciana (PROMETEO/2014/011). UMH-CSIC. IP: Antonio Ferrer Montiel.

Sensibilización algésica de nociceptores en dolor crónico: mecanismos e intervención farmacológia. 23/06/2015 - Proyectos de I+D+I "RETOS DE LA SOCIEDAD" - MINECO 2015 (SAF2015-66275-C2-1-R). UMH-CSIC Ministerio de Economia y Competitividad. IP: Antonio Ferrer Montiel.

Private Funding.

Contrato para la realización del trabajo "Modelización molecular de interacciones proteína-proteína en el receptor muscarínico de acetilcolina". Funded by Antalgenics SL (ANTALGENICS2.15T; 30/04/2016). IP: G. Fernandez-Ballester.

Adenda al contrato para la realización del trabajo "Modelización molecular de interacciones proteína-proteína en el receptor muscarínico de acetilcolina". Funded by Antalgenics SL (ANTALGENICS4.16D; 28/10/2016). IP: G. Fernandez-Ballester.

Identificación y desarrollo de productos cosméticos. LIPOTEC.

Optimización de la expresión y purificación de péptidos recombinantes procedentes del veneno de escorpión *Rhopalurus junceus* en sistemas procariotas y caracterización de su actividad biológica. LABIOFAM.

Desarrollo de una vacuna de betanodavirus para lubina. El objetivo del proyecto es el desarrollo de una vacuna inactivada contra el *Betanodavirus* RG causante de la enfermedad de la necrosis nerviosa viral (viral nervous necrosis, VNN) o encefalopatía y retinopatía viral (viral encephalopathy and retinopathy, VER), destinada a alevines y especímenes adultos de lubina (*Dicentrarchus labrax* L.). HIPRA.

Technical Services and Assistance.

Antonio Ferrer. Technical Assistance to AntalGenics SL.

Scientific Society Councils: R&D Management.

Co-manager of grants in the R&D National Plan (Pharmacological and Delivery Sciences) at MINECO.

Scientific Society Councils.

Sociedad Española de Biofísica. (2014-2018). A. Ferrer. President.

Editorial Boards.

Advances in Pharmacological Sciences (2010-2015). A. Ferrer.

The Open Journal of Pain (2011-2015). A. Ferrer.

Frontiers in Pharmacology (2014-2015) A. Ferrer.

Scientific Reports (2014-2016). A. Fernandez-Carvajal.

Frontiers in Physiology (2015-2016) A. Fernandez-Carvajal.

Antiviral Strategies.

Group name: ANTIVIRAL STRATEGIES.

The group of Virology at the IBMC was established fourteen years ago. The group members have proven expertise over 20 years in the field of viral diseases of fish in aquaculture. The group's interest is focused on the study of viruses, fish immune response related to virus infections and antiviral strategies for disease prevention and treatment:

- Study of the early steps of rhabdovirus infections.
- Design of new antivirals using combinatorial chemistry or molecules related to the innate immune response such as AMPs (antimicrobial peptides).
- Development of environmentally friendly DNA vaccines. Characterization of the immune response induced by DNA vaccines using genomic and proteomic approaches (microarrays) to determine the molecular bases of protection conferred by these vaccines.

Staff.

Luis Pérez García-Estañ

Postdoctoral Fellows.

Alberto Falcó Gracia

Ph.D Students.

Regla María Medina Gali

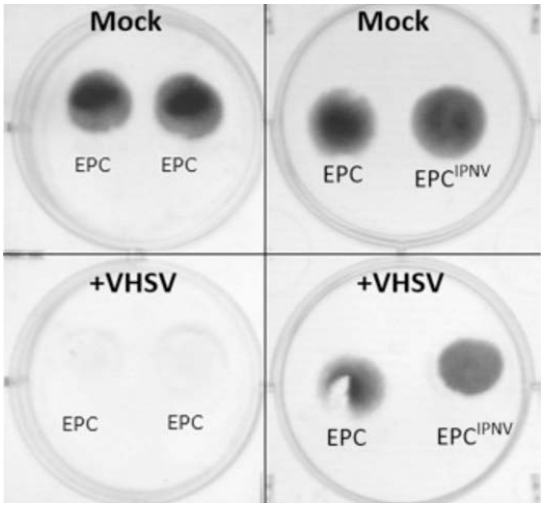
Melissa Belló Pérez

Technicians.

Beatriz Bonmatí

Publications.

Ricardo Parreño, Susana Torres, Lucía Almagro, Melissa Belló-Perez, Amparo Estepa y Luis Perez. Induction of viral interference by IPNV-carrier cells on target cells: a cell co-culture study. Fish Shellfish Immunol. (2016) 58: 483-489.



Bello, M., Falco, A., Medina Gali, R.M., Encinar, J.A., Novoa, B., Perez, L., Coll, J. Structure and functionalities of the human c-reactive protein compared to the zebrafish multigene family of c-reactive-like proteins. Dev Comp Immunol. 2016; 69:33-40.

Governmental Projects and Funding.

Project: Buscando aplicaciones para la memoria innata ("trained immunity") en peces: inmunomoduladores, agentes terapeùticos y vacunas. Proyectos de I+D+I "Retos de la sociedad" - MINECO 2014\AGL2014-51773-C3-1-R.

Science dissemination: outreach activities.

Luis Perez, Vacunas para ¿virus de peces?, artículo en revista Sociedad Española de Virología vol 19 nº2 (2016).

Luis Perez y José A. López Guerrero, 2016. Conferencia Zika, Ebola y Chikunguña, los virus que salieron del bosque, FeCiTElx 2016, Elche.

Group name: ENVELOPED VIRUSES. BIOMEMBRANES, PROTEINS AND DESIGN ON NOVEL ANTIVIRALS.

Among the pathogens which cause the higher rates of mortality and morbidity on humans and animals we can name the viruses. However, in the vast majority of cases, there are no vaccines or effective therapeutic treatments. Flaviviridae constitute a large family of viruses to which medically highly relevant human pathogens belong. Viruses such as the hepatitis C virus, the Yellow Fever Virus, West Nile virus, Tick-Borne Encephalitis Viruses, Zika and Dengue belong to this family. Dengue (DENV), as well as Zika (ZIKV), cause the most prevalent arthropod-borne viral disease among humans affecting millions of people per year. These diseases have evolved from a sporadic occurrence to a global public health problem. The number of reported cases is increasing geometrically due to environmental and geographical changes and many countries, including ours, have a direct risk to them. Significantly, all processes inherent to the viral replication cycle are directly or indirectly related to membrane systems or membranes derived from them. Anything that might interfere with any one of these processes would be potentially useful in ensuring that the virus cannot get in or out of the cell. Our group aims to study the structure and interaction with different types of model biomembrane systems of several peptide domains derived from the structural and non-structural proteins of DENV and ZIKV viruses. Our goal will be to distinguish and correlate the effects on both the peptides and the membrane components, with the specific aims of obtaining, on the one hand, the knowledge of the molecular mechanism of the biological function of the original proteins and on the other, effective antiviral and bioactive molecules against them. Relaying on the knowledge we have about the structural and non-structural proteins of DENV, our experimental approach and objectives will consist of using in silico molecular dynamics to find the specific interacting three dimensional structure of selected peptides of DENV and ZIKV with biomembrane model systems, in vitro obtain exhaustive information about its structure and specific lipid interaction, in silico screening and peptide docking methodologies to obtain antiviral peptides and bioactive molecules against those obtained structure, and test them to check their effectivity using different model biomembrane compositions. These data will permit us the development of new leading compounds useful for improved combined therapies in order to achieve the ultimate goal, eradicate the DENV and ZIKV viral infections.

Staff.

José Villalaín Boullón

Vicente Galiano Ibarra

Postdoctoral Fellows.

Enmanuel Fajardo Sánchez

Publications.

Location of the bioactive pentacyclic triterpene ursolic acid in the membrane. A molecular dynamics study. Fajardo-Sánchez E, Galiano V, Villalaín J. J Biomol Struct Dyn. 2016 Sep 12:1-13. doi: 10.1080/07391102.2016.1229219.

Molecular dynamics study of the membrane interaction of a membranotropic dengue virus C protein-derived peptide. Fajardo-Sánchez E, Galiano V, Villalaín J. J Biomol Struct Dyn. 2016 May 21:1-12. doi: 10.1080/07391102.2016.1179595.

The Location of the Protonated and Unprotonated Forms of Arbidol in the Membrane: A Molecular Dynamics Study. Galiano V, Villalaín J. J Membr Biol. 2016 Jun;249(3):381-91. doi: 10.1007/s00232-016-9876-3.

Governmental Projects and Funding.

Título del proyecto: Caracterización de la interacción proteína-membrana en el virus del dengue. Una herramienta para el desarrollo de antivirales. Entidad financiadora: MEC - BFU2013-43198-P. 1-1-2014- 31-12-2017. IP. José Villalaín.

Number of Congress Communications.

National contributions: 3 Poster.

Group name: FISH ERYTHROCYTES IN ANTIVIRAL IMMUNOLOGY.

Fish are the phylogenetically oldest vertebrate group with an immune system with clear similarities to the immune system of mammals. However, it is an actual matter of fact that the current knowledge of the fish immune system seems to lack the key piece to complete the puzzle.

In 1953 Nelson described a new role of human red blood cells (RBCs) which would go beyond the simple transport of O2 to the tissues. This new role, involved in the defence against microbes, described the antibody and complement-dependent binding of microbial immune complexes to RBCs. Regardless of the importance of this finding in the field of microbial infection, this phenomenon has been poorly evaluated. Just recently, a set of biological processes relevant to immunity have been described in the RBCs of a diverse group of organisms, which include: pathogen recognition, pathogen binding and clearance and cytokines production.

Furthermore, it has been demonstrated that nucleated erythrocytes from fish and avian species develop specific responses to different pathogen associated molecular patterns and produce soluble factors that modulate leukocyte activity.

In the light of these pieces of evidences, and in an attempt to improve the knowledge of the immune mechanism(s) responsible for fish protection against viral infections, we raised the question: could nucleated fish erythrocytes be the key mediators of the antiviral responses? To answer this question we decided to focus our work on the evaluation of the crosstalk between red and white blood cells in the scenario of fish viral infections and prophylaxis. For that we chose a working model composed of the rainbow trout, the viral haemorrhagic septicaemia virus (VHSV) and the glycoprotein G of VHSV (GVHSV), the antigen encoded by this DNA vaccine.

Staff.

María del Mar Ortega-Villaizán Romo

Postdoctoral Fellows.

Verónica Chico Gras

Ph.D students.

Iván Nombela Díaz

Sara Puente Marín

Publications.

Ortega-Villaizan M, Chico V, Martinez-Lopez A, Garcia-Valtanen P, Coll JM, Estepa A. Development of new therapeutical/adjuvant molecules by pepscan mapping of autophagy and IFN inducing determinants of rhabdoviral G proteins. Mol Immunol. 2016 Feb; 70:118-24. doi: 10.1016/j.molimm.2015.10.008.

Governmental Projects and Funding.

ERC Starting Grant 2014. Proyecto: BloodCellsCrosstalk. "The Crosstalk Between Red and White Blood Cells: The case of fish". GA639249. European Commission.

Number of Congress Communications.

National contributions: 2 Oral presentations.

Molecular and Cellular Oncology.

Group name: MOLECULAR AND CELLULAR ONCOLOGY.

The main objectives of our research group are, first, the study of the molecular mechanisms associated to chemo and radio resistance in cancer, and second, the search of new therapeutical strategies for the treatment of chemo and radiorresistant tumours. We propose different experimental approaches to raise these objectives:

1. Development of celular models closer to the patient, allowing ex vivo tests of the treatments.
2. Development of the several models in order to determine the presence of tumour stem cells in primary cultures.
3. Use of novel therapies such as epigenetic and enzimatic therapies, in celular models from glioblastoma and pancreatic carcinoma.
4. Study of signal transduction pathways involved in resistance acquisition in glioblastoma and pancreatic carcinoma. This experimental approach allows the identification of genes involved in this process that can be considered as putative therapeutical targets.

During the last years, nanotechnology development has gained an important boom as a putative therapeutical approach for the treatment of several tumours. The use of immunodirected nanoparticles, will allow:

- To increase of the local doses and to decrease of the secondary effects.
- To direct the treatments to celular subpopulations of interest on the tumour, such as tumour stem cells or stroma cells.
- To combine and direct different and novel therapeutical strategies against the tumours of interest, such as epigenetic and enzimatic therapies.
- To explore the possibilities of these nanoparticles to potentiate the immunogenic effects observed with classical chemotherapeutical treatments as well as with radiotherapical treatments.

Staff.

Miguel Saceda Sánchez

Mª Isabel Martínez-Lacaci Fortuny

Mª Pilar García Morales

Ph.D Students.

María Fuentes Baile

María Paz Ventero Martin

Organization of Meetings.

II Jornada de Investigación Biomédica HGUE-IBMC, 3 de Octubre 2016.

Invited talks and courses.

Aplicación de las técnicas de acoplamiento molecular para el desarrollo de nuevos fármacos antitumorales. II Jornada de Investigación Biomédica HGUE-IBMC.

Number of Congress Communications.

International contributions: 1 poster presentations.

Governmental Projects and Funding.

Título del proyecto: Desarrollo de inhibidores de PTK6 como posibles nuevos agentes terapéuticos en cáncer. Evaluación de su potencialidad en modelos celulares de tumores de mama, páncreas y colon. Entidad financiadora: FIS PI01202025. Duración, desde: 2013 hasta: 2016. 65,000 €, IP: Dr. Miguel Saceda.

Título del proyecto: Terapias antitumorales basadas en nanotecnología. Ayudas para la captación de proyectos europeos u otros programas de ámbito internacional (2016). APE/2016/028. Generalitat Valenciana. IP: Dr. Miguel Saceda.

Private funding: Contracts.

Título del proyecto: Nanotecnología, terapia enzimática y cribado de nuevas moléculas para la optimización del tratamiento radioterápico en tumores quimio y radio resistentes. Entidad Financiadora: Fundación ERESA SL. 2016 - 2017. 12,000 €, IP: Dr. Miguel Saceda.

Donación de AFECANCER (Asociación de familiares y pacientes de cáncer de Torrevieja) para investigación en cáncer. 1,500 €.

PhD THESES (2016).

04/11/2016. **Interaction between conjugated polylectrolytes and biological systems: characterization and biotechnological applications**. Autor: Zehra Kahveci. Dirección: Carmen Reyes Mateo Martínez.

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1335159

29/07/2016. **Estudios de conducción y selectividad iónicas basados en un canal de potasio modelo: KCSA**. Autor: Estefanía Montoya Díaz. Dirección: Dres. Jose Manuel González Ros, Jose Antonio Poveda Larrosa y Asia Fernández Carvajal.

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1294119

11/07/2016. **Characterization and evaluation of TRPV1 and TRPM8 antagonists as potential therapeutic tools for treating pain**. Autor: Roberto de la Torre Martínez. Dirección: Dres. Antonio Vicente Ferrer Montiel y Asia Fernandez Carvajal.

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1281105

12/05/2016. **Differential mechanism of TRPV1 sensitization in peptidergic and nonpeptidergic nociceptors**. Autor: Sakthikumar Mathivananna. Dirección: Dr. Antonio Vicente Ferrer Montiel.

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1257315

29/02/2016. **Efecto modulador de bifidobacterium pseudocatenulatum CECT 7765 sobre la respuesta inflamatoria y la translocación bacteriana en la cirrosis**. Autor: Alba Moratalla Fernández. Dirección: Dres. Rubén Frances Guarinos y José Such Ronda.

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1228806

22/01/2016. **Identification and characterisation of Whirlin as a novel modulator of TRPV1**. Autor: Maria Grazia Ciardo. Dirección: Dres. Antonio Ferrer Montiel y Rosa Planells Cases.

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1212444

SEMINARS (2016).

Título: **I+D para fortalecimiento de la empresa en el sector cosmético y de producto sanitario**. Ponente / Institución: María Matabuena de Yzaguirre. INVITROTECNIA S.L. Viernes 18 de noviembre de 2016.

Título: **El desarrollo de estrategias antirretrovirales como paradigma de búsqueda de nuevas terapias antivirales**. Ponente / Institución: Dra. Mª Eugenia González Portal. Instituto de Salud Carlos III, Madrid. Viernes 11 de noviembre de 2016.

Título: **Subphthalocyanines: Singular aromatic non-planar molecules**. Ponente / Institución: Tomás Torres Cebada. Dpto. Química Orgánica, Universidad Autónoma de Madrid. Viernes 28 de octubre de 2016.

Título: **Diseño de péptidos transmembrana para aplicaciones oncológicas**. Ponente / Institución: Francisco Barrera Olivares. Universidad de Tennessee. Martes, 20 de septiembre 2016.

Título: **Exploring the pan-genome of pathogenic bacterial species for the identification of novel antimicrobial targets and vaccine candidates**. Ponente / Institución: Xavier Daurà. Institute of Biotechnology and Biomedicine. Universitat Autònoma de Barcelona. Viernes, 10 de junio 2016.

Título: **The role of spatiotemporal heterogeneity in the regulation of celular function**. Ponente / Institución: Carlo Manzo. ICFO (Instituto de Ciencias Fotónicas) - Barcelona. Viernes 3 de junio de 2016.

Título: **Poros no constitutivos, inducidos por péptidos y proteínas**. Ponente / Institución: Jesús Salgado. Universidad de Valencia. Viernes 27 de mayo de 2016.

Título: **Cómo escribir un gran artículo de investigación, y conseguir que sea aceptado en una buena revista**. Ponente / Institución: Anthony Newman. Editor Senior, Departamento de Ciencias de Vida, Elsevier, Amsterdam, Países Bajos. Miércoles 18 de mayo de 2016.

Título: **Fullerenes for Bio-Medical Applications: The case of Ebola Virus Infection**. Ponente / Institución: Nazario Martin. Departamento de Química Orgánica, Facultad de Química, Universidad Complutense e IMDEA-Nanociencia, Madrid, Spain. Viernes 13 de mayo de 2016.

Título: **Electrodifusión en poros bacteriales: una multitud de fenómenos más allá de la difusión pasiva y débil selectividad iónica**. Ponente / Institución: Vicente Aguillella. Departamento de Física. Universidad Jaume I, Castellón. Viernes 6 de mayo de 2016.

Título: **Fagoterapia y enzibióticos: nuevas armas contra las infecciones bacterianas**. Ponente / Institución: Dr. Pedro García González. Centro de Investigaciones Biológicas (CSIC-Madrid). Viernes 22 de abril de 2016.

Título: **Evolución pato-adaptativa en el sistema respiratorio humano: infección por *Haemophilus influenzae* y enfermedad pulmonar obstructiva crónica (EPOC)**. Ponente / Institución: Dra. Junkal Garmendia. Instituto de Agrobiotecnología (CSIC-UPNA-Gobierno de Navarra). Viernes 8 de abril de 2016.

Título: **Atomización electro-hidrodinámica de líquidos: historia, presente y futuro**. Ponente / Institución: Dr. Ignacio González Loscertales. Universidad de Málaga. Viernes 26 de febrero de 2016.

Título: **Cómo ve y responde una bacteria a la luz: el descubrimiento de una nueva familia de fotorreceptores**. Ponente / Institución: Dra. Montserrat Elías. Universidad de Murcia. Viernes 15 de enero de 2016.

ANNUAL REPORT 2016

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